

REMARKS: CLAIM REJECTION UNDER 35 U.S.C. § 103(a)

Claims 1-10, 12, and 13 stand rejected under 35 U.S.C. §103(a) (“Section 103(a)”) as obvious over U.S. Patent No. 6,436,449 (issued Aug. 20, 2002) (“Gidlund”). Applicant respectfully submits that Gidlund fails to teach the claim limitations recited in the present application because 1) Gidlund teaches the use of extracts not juice; and 2) Gidlund teaches methods for treating tinnitus not methods for treating pain through selective COX-2 inhibition. M.P.E.P. § 2142.

1. Gidlund Teaches the Use of Extracts Not Juice

The independent claims of the present invention include “juice” as a limitation. Because Gidlund teaches the use of extracts not juice, Gidlund fails to teach every claimed limitation of the present invention. Gidlund teaches use of an extract derived from the fruits, leaves, the bark or the roots of *Morinda citrifolia* for the manufacture of a medicament for the treatment of a mammal suffering from tinnitus. The present invention claims a method of administering juice to reduce pain through selective COX-2 inhibition. Isolating an extract from the fruit and ingesting it to ameliorate tinnitus, as taught in Gidlund, would not produce the desired effect of the claim method of the present application.

Examiner indicates that “[t]he Gidlund reference clearly states that the term ‘extract’ as used therein encompasses the juice of *Morinda citrifolia* as pressed from the fruit of that plant, which may be further processed as known in the art”(emphasis added). In fact Column 4 lines 26-30 of the Gidlund reference indicate: “[t]he extract from the fruit may be either liquid, i.e. the juice as pressed from the fruits and treated in the way conventional to the art, or solid ...” Column 4 lines 26-30 teach that the extract administered to ameliorate tinnitus, may be extracted

from the juice and administered in a liquid form. Column 4 lines 26-30 do not teach administration of juice.

The administration of an extract is different from the administration of juice. Gidlund teaches administering extracts derived from *Morinda citrifolia* juice not administration of the juice itself. Extraction is the process of selecting for and isolating certain ingredients present in the whole. Administering selected ingredients instead of other non-selected ingredients would produce different biological effects.<sup>1</sup> For example, administering potassium instead of myristic acid would produce different biological effects, and administering whole *Morinda citrifolia* fruit instead of potassium only would produce different biological effects.

## 2. Gidlund Does Not Teach a Method for Reducing Pain By Selective COX-2 Inhibition

The difference between treatment of pain and selective COX-2 inhibition is patentable. COX-2 expression is associated with pain and inflammation. COX-1 is a constitutively active enzyme responsible, among other things, for maintaining the mucosal lining of the stomach. When COX-2 is inhibited, pain is reduced. When COX-1 is inhibited, patients experience uncomfortable side effects including gastric ulcers.

Compounds or formulations, which favorably influence pain, do not have a reasonable probability for reducing pain by selective COX-2 inhibition. For example, a popular treatment of chronic pain and inflammation involves the use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs inhibit both COX-2 and COX-1. While NSAIDs have been effective in

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<sup>1</sup> The fruit of the *Morinda citrifolia* plant is comprised of several different ingredients. For example the fruit of *Morinda citrifolia* is comprised of: acetic acid, asperuloside, butanoic acid, benzoic acid, benzyl alcohol, 1-butanol, caprylic acid, decanoic acid, (E)-6-dodeceno-gamma-lactone, (Z,Z,Z)-8,11,14-eicosatrienoic acid, elaidic acid, ethyl decanoate, ethyl hexanoate, ethyl octanoate, ethyl palmitate, (Z)-6-(ethylthiomethyl) benzene, eugenol, glucose, heptanoic acid, 2-heptanone, hexanal, hexanamide, hexanedioic acid, hexanoic acid (hexoic acid), 1-hexanol, 3-hydroxy-2-butanone, lauric acid, limonene, linoleic acid, 2-methylbutanoic acid, 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, methyl decanoate, methyl elaidate, methyl hexanoate, methyl 3-methylthio-propanoate, methyl octanoate, methyl oleate, methyl palmitate, 2-methylpropanoic acid, 3-methylthio-propanoic acid, myristic acid, nonanoic acid, octanoic acid (octoic acid), oleic acid, palmitic acid, potassium, scopoletin, undecanoic acid, (Z,Z)-2,5-undecadien-1-ol, and vomifol.

reducing inflammation and pain, NSAIDs have a number of adverse side effects. The major side effects of NSAIDs are gastrointestinal related. In order to provide relief pain associated with COX-2 without inhibiting COX-1, drug companies have attempted to produce selective COX-2 inhibitors (e.g. VIOXX).

Applicants claim limitation for “varying the concentration” of doses of *Morinda citrifolia* based on several factors in order to limit undesired COX-1 inhibition relative to COX-2 inhibition is not obvious in view of Gidlund’s disclosure. *See Claims 1 and 12.* Applicants’ disclosure demonstrates the importance and non-obviousness of administering the appropriate concentration of *Morinda citrifolia*. Applicants’ experiments provide the non-obvious discovery that at some concentrations, selective COX-2 inhibition was achieved, and at other concentrations it was not. Specification, pg. 15. The Applicants indicated, “the data suggests the surprising result that in some circumstances ‘less’ *Morinda citrifolia* juice provides ‘more’ inhibition selectivity.” Specification, pg. 15. Applicants’ disclosure shows that COX-2 selectivity is undermined by excessive, increased concentrations. Specification, pg. 15. It is only after the inherent COX-1 inhibiting qualities of *Morinda citrifolia* are limited by the methods of the present invention that selective COX-2 inhibition occurs.

CONCLUSION

Because the cited prior art fails to teach or suggest all claim limitations of the present invention, Applicants submit that the present invention is not obvious. Applicants submit that the claims are now in condition for allowance. Accordingly, Applicants request favorable reconsideration. If the Examiner has any questions or concerns regarding this communication, the Examiner is invited to call the undersigned.

DATED this 23 day of June, 2005.

Respectfully submitted,



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